SEQUENCE LISTING 10> SHONE, Clifford Charles SUTTON, John Mark HALLIS, Bassam SILMAN, Nigel <120> Delivery of Superoxide Dismutase to Neuronal Cells <130> 1581.0800000 <140> 09/831,050 <141> 1999-11-05 <150> PCT/GB99/03699 <151> 1998-11-05 <160> 14 <170> PatentIn Ver. 2.1 <210> 1 <211> 204 <212> PRT <213> Bacillus caldotenax Met Pro Phe Glu Leu Pro Ala Leu Pro Tyr Pro Tyr Asp Ala Leu Glu Pro His Ile Asp Lys Glu Thr Met Asn Ile His His Thr Lys His His 25 Asn Thr Tyr Val Thr Asn Leu Asn Ala Leu Glu Gly His Pro Asp Leu Gln Asn Lys Ser Leu Glu Glu Leu Leu Ser Asn Leu Glu Ala Leu Pro Glu Ser Ile Arg Thr Ala Val Arg Asn Asn Gly Gly His Ala Asn His Ser Leu Phe Trp Thr Ile Leu Ser Pro Asn Gly Gly Glu 85 Pro Thr Gly Glu Leu Ala Glu Ala Ile Asn Lys Lys Phe Gly Ser Phe 105 Thr Ala Phe Lys Asp Glu Phe Ser Lys Ala Ala Ala Gly Arg Phe Gly Ser Gly Trp Ala Trp Leu Val Val Asn Asn Gly Glu Leu Glu Ile Thr 135 Ser Thr Pro Asn Gln Asp Ser Pro Ile Met Glu Gly Lys Thr Pro Ile 145 150 155 160 Leu Gly Leu Asp Val Trp Glu His Ala Tyr Tyr Leu Lys Tyr Gln Asn Arg Arg Pro Glu Tyr Ile Ala Ala Phe Trp Asn Ile Val Asn Trp Asp

Glu Val Ala Lys Arg Tyr Ser Glu Ala Lys Ala Lys

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<210> 2
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<211> 204

<212> PRT

<213> Bacillus stearothermophilus

<400> 2

Met Pro Phe Glu Leu Pro Ala Leu Pro Tyr Pro Tyr Asp Ala Leu Glu 1 5 10 15

Pro His Ile Asp Lys Glu Thr Met Asn Ile His His Thr Lys His His 20 25 30

Asn Thr Tyr Val Thr Asn Leu Asn Ala Ala Leu Glu Gly His Pro Asp 35 40 45

Leu Gln Asn Lys Ser Leu Glu Glu Leu Leu Ser Asn Leu Glu Ala Leu
50 60

Pro Glu Ser Ile Arg Thr Ala Val Arg Asn Asn Gly Gly His Ala
65 70 75 80

Asn His Ser Leu Phe Trp Thr Ile Leu Ser Pro Asn Gly Gly Glu
85 90 95

Pro Thr Gly Glu Leu Ala Asp Ala Ile Asn Lys Lys Phe Gly Ser Phe
100 105 110

Thr Ala Phe Lys Asp Glu Phe Ser Lys Ala Ala Ala Gly Arg Phe Gly
115 120 125

Ser Gly Trp Ala Trp Leu Val Val Asn Asn Gly Glu Leu Glu Ile Thr 130 135 140

Ser Thr Pro Asn Gln Asp Ser Pro Ile Met Glu Gly Lys Thr Pro Ile 145 150 155 160

Leu Gly Leu Asp Val Trp Glu His Ala Tyr Tyr Leu Lys Tyr Gln Asn

Arg Arg Pro Glu Tyr Ile Ala Ala Phe Trp Asn Val Val Asn Trp Asp 180 185 190

Glu Val Ala Lys Arg Tyr Ser Glu Ala Lys Ala Lys 195 200

<210> 3

<211> 1067

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:construct

<400> 3

Met Pro Phe Glu Leu Pro Ala Leu Pro Tyr Pro Tyr Asp Ala Leu Glu
1 5 10 15

Pro His Ile Asp Lys Glu Thr Met Asn Ile His His Thr Lys His His 20 25 30

Asn Thr Tyr Val Thr Asn Leu Asn Ala Ala Leu Glu Gly His Pro Asp
35 40 45

Leu Gln Asn Lys Ser Leu Glu Glu Leu Leu Ser Asn Leu Glu Ala Leu Pro Glu Ser Ile Arg Thr Ala Val Arg Asn Asn Gly Gly His Ala Asn His Ser Leu Phe Trp Thr Ile Leu Ser Pro Asn Gly Gly Glu Pro Thr Gly Glu Leu Ala Asp Ala Ile Asn Lys Lys Phe Gly Ser Phe 105 Thr Ala Phe Lys Asp Glu Phe Ser Lys Ala Ala Gly Arg Phe Gly Ser Gly Trp Ala Trp Leu Val Val Asn Asn Gly Glu Leu Glu Ile Thr 135 Ser Thr Pro Asn Gln Asp Ser Pro Ile Met Glu Gly Lys Thr Pro Ile Leu Gly Leu Asp Val Trp Glu His Ala Tyr Tyr Leu Lys Tyr Gln Asn Arg Arg Pro Glu Tyr Ile Ala Ala Phe Trp Asn Val Val Asn Trp Asp 185 Glu Val Ala Lys Arg Tyr Ser Glu Ala Lys Ala Lys Gln Arg Ser Cys Gly Leu Val Pro Arg Gly Ser Gly Pro Gly Ser Ala Leu Asn Asp Leu 215 Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp 230 235 Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr 250 Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu Asp Leu Ile Gln Gln 265 Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile 280 285 Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn 295 Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr 315 Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg 330 Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg 340 345 Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp

390

Ile Thr Ile Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala 425 Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln 455 Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val 475 Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile 490 Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu 505 Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu 535 Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn 555 Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val 570 Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys 585 Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu 600 Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu 615 Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser Thr Phe Thr Glu Tyr 630 635 Ile Lys Asn Ile Ile Asn Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser 645 Asn His Leu Ile Asp Leu Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys Ile Glu Val Ile Leu Lys Asn Ala Ile Val 695 Tyr Asn Ser Met Tyr Glu Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile 715 Pro Lys Tyr Phe Asn Ser Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly 745

Glu Ile Ile Trp Thr Leu Gln Asp Thr Gln Glu Ile Lys Gln Arg Val 755 760 765

Val Phe Lys Tyr Ser Gln Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg 770 775 780

Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile
785 790 . 795 800

Tyr Ile Asn Gly Arg Leu Ile Asp Gln Lys Pro Ile Ser Asn Leu Gly 805 810 815

Asn Ile His Ala Ser Asn Asn Ile Met Phe Lys Leu Asp Gly Cys Arg 820 825 830

Asp Thr His Arg Tyr Ile Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys 835 840 845

Glu Leu Asn Glu Lys Glu Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn 850 860

Ser Gly Ile Leu Lys Asp Phe Trp Gly Asp Tyr Leu Gln Tyr Asp Lys 865 870 875 880

Pro Tyr Tyr Met Leu Asn Leu Tyr Asp Pro Asn Lys Tyr Val Asp Val 885 890 895

Asn Asn Val Gly Ile Arg Gly Tyr Met Tyr Leu Lys Gly Pro Arg Gly 900 905 910

Ser Val Met Thr Thr Asn Ile Tyr Leu Asn Ser Ser Leu Tyr Arg Gly 915 920 925

Thr Lys Phe Ile Ile Lys Lys Tyr Ala Ser Gly Asn Lys Asp Asn Ile 930 935 940

Val Arg Asn Asn Asp Arg Val Tyr Ile Asn Val Val Lys Asn Lys 945 950 955 960

Glu Tyr Arg Leu Ala Thr Asn Ala Ser Gln Ala Gly Val Glu Lys Ile 965 970 975

Leu Ser Ala Leu Glu Ile Pro Asp Val Gly Asn Leu Ser Gln Val Val 980 985 990

Val Met Lys Ser Lys Asn Asp Gln Gly Ile Thr Asn Lys Cys Lys Met 995 1000 1005

Asn Leu Gln Asp Asn Asn Gly Asn Asp Ile Gly Phe Ile Gly Phe His 1010 1015 1020

Gln Phe Asn Asn Ile Ala Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg 1025 1030 1035 1040

Gln Ile Glu Arg Ser Ser Arg Thr Leu Gly Cys Ser Trp Glu Phe Ile 1045 1050 1055

Pro Val Asp Asp Gly Trp Gly Glu Arg Pro Leu 1060 1065

<sup>&</sup>lt;210> 4

<sup>&</sup>lt;211> 1070

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:construct

<400> 4

Met Pro Phe Glu Leu Pro Ala Leu Pro Tyr Pro Tyr Asp Ala Leu Glu 1 5 10 15

Pro His Ile Asp Lys Glu Thr Met Asn Ile His His Thr Lys His His 20 25 30

Asn Thr Tyr Val Thr Asn Leu Asn Ala Ala Leu Glu Gly His Pro Asp 35 40 45

Leu Gln Asn Lys Ser Leu Glu Glu Leu Leu Ser Asn Leu Glu Ala Leu 50 55 60

Pro Glu Ser Ile Arg Thr Ala Val Arg Asn Asn Gly Gly His Ala 65 70 75 80

Asn His Ser Leu Phe Trp Thr Ile Leu Ser Pro Asn Gly Gly Glu 85 90 95

Pro Thr Gly Glu Leu Ala Asp Ala Ile Asn Lys Lys Phe Gly Ser Phe
100 105 110

Thr Ala Phe Lys Asp Glu Phe Ser Lys Ala Ala Ala Gly Arg Phe Gly 115 120 125

Ser Gly Trp Ala Trp Leu Val Val Asn Asn Gly Glu Leu Glu Ile Thr 130 135 140

Ser Thr Pro Asn Gln Asp Ser Pro Ile Met Glu Gly Lys Thr Pro Ile 145 150 155 160

Leu Gly Leu Asp Val Trp Glu His Ala Tyr Tyr Leu Lys Tyr Gln Asn 165 170 175

Arg Arg Pro Glu Tyr Ile Ala Ala Phe Trp Asn Val Val Asn Trp Asp 180 185 190

Glu Val Ala Lys Arg Tyr Ser Glu Ala Lys Ala Lys Gln Arg Ser Cys 195 200 205

Gly Leu Val Pro Arg Gly Ser Gly Pro Gly Ser Lys Ala Pro Gly Ile 210 215 220

Cys Ile Asp Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys Asn 225 230 235 240

Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn Thr 245 250 255

Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu Ile Leu 260 265 270

Asp Thr Asp Leu Ile Ser Lys Ile Glu Leu Pro Ser Glu Asn Thr Glu 275 280 285

Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val Tyr Glu Lys Gln Pro 290 295 300

Ala Ile Lys Lys Ile Phe Thr Asp Glu Asn Thr Ile Phe Gln Tyr Leu 305 310 315 320

Tyr Ser Gln Thr Phe Pro Leu Asp Ile Arg Asp Ile Ser Leu Thr Ser 325 330 335

Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn Lys Val Tyr Ser Phe Phe 345 Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly Leu 360 Phe Ala Gly Trp Val Lys Gln Ile Val Asn Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala Asp Ile Ser Leu Ile Val 395 Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly Ala Ser Ile Leu Leu Glu 425 Phe Ile Pro Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu Glu Ser Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile Val 475 470 Ala Gln Trp Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile 505 Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn 535 Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu Asn 585 Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr Ile Met Pro Phe Asp Leu Ser Ile Tyr Thr Asn 615 Asp Thr Ile Leu Ile Glu Met Phe Asn Lys Tyr Asn Ser Glu Ile Leu 625 630 635 Asn Asn Ile Ile Leu Asn Leu Arg Tyr Lys Asp Asn Asn Leu Ile Asp Leu Ser Gly Tyr Gly Ala Lys Val Glu Val Tyr Asp Gly Val Glu Leu Asn Asp Lys Asn Gln Phe Lys Leu Thr Ser Ser Ala Asn Ser Lys Ile 675 680 685

Arg Val Thr Gln Asn Gln Asn Ile Ile Phe Asn Ser Val Phe Leu Asp 690 695 Phe Ser Val Ser Phe Trp Ile Arg Ile Pro Lys Tyr Lys Asn Asp Gly Ile Gln Asn Tyr Ile His Asn Glu Tyr Thr Ile Ile Asn Cys Met Lys Asn Asn Ser Gly Trp Lys Ile Ser Ile Arg Gly Asn Arg Ile Ile Trp 745 Thr Leu Ile Asp Ile Asn Gly Lys Thr Lys Ser Val Phe Phe Glu Tyr Asn Ile Arg Glu Asp Ile Ser Glu Tyr Ile Asn Arg Trp Phe Phe Val Thr Ile Thr Asn Asn Leu Asn Asn Ala Lys Ile Tyr Ile Asn Gly Lys Leu Glu Ser Asn Thr Asp Ile Lys Asp Ile Arg Glu Val Ile Ala Asn 805 Gly Glu Ile Ile Phe Lys Leu Asp Gly Asp Ile Asp Arg Thr Gln Phe 825 Ile Trp Met Lys Tyr Phe Ser Ile Phe Asn Thr Glu Leu Ser Gln Ser Asn Ile Glu Glu Arg Tyr Lys Ile Gln Ser Tyr Ser Glu Tyr Leu Lys Asp Phe Trp Gly Asn Pro Leu Met Tyr Asn Lys Glu Tyr Tyr Met Phe Asn Ala Gly Asn Lys Asn Ser Tyr Ile Lys Leu Lys Lys Asp Ser Pro Val Gly Glu Ile Leu Thr Arg Ser Lys Tyr Asn Gln Asn Ser Lys Tyr Ile Asn Tyr Arg Asp Leu Tyr Ile Gly Glu Lys Phe Ile Ile Arg Arg 915 920 Lys Ser Asn Ser Gln Ser Ile Asn Asp Asp Ile Val Arg Lys Glu Asp Tyr Ile Tyr Leu Asp Phe Phe Asn Leu Asn Gln Glu Trp Arg Val Tyr 950 Thr Tyr Lys Tyr Phe Lys Lys Glu Glu Lys Leu Phe Leu Ala Pro 965 Ile Ser Asp Ser Asp Glu Phe Tyr Asn Thr Ile Gln Ile Lys Glu Tyr Asp Glu Gln Pro Thr Tyr Ser Cys Gln Leu Leu Phe Lys Lys Asp Glu 1000 Glu Ser Thr Asp Glu Ile Gly Leu Ile Gly Ile His Arg Phe Tyr Glu Ser Gly Ile Val Phe Glu Glu Tyr Lys Asp Tyr Phe Cys Ile Ser Lys

1030

Trp Tyr Leu Lys Glu Val Lys Arg Lys Pro Tyr Asn Leu Lys Leu Gly
1045 1050 1055

Cys Asn Trp Gln Phe Ile Pro Lys Asp Glu Gly Trp Thr Glu 1060 1065 1070

<210> 5

<211> 1059

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:construct

<400> 5

Met Pro Phe Glu Leu Pro Ala Leu Pro Tyr Pro Tyr Asp Ala Leu Glu
1 5 10 15

Pro His Ile Asp Lys Glu Thr Met Asn Ile His His Thr Lys His His
20 25 30

Asn Thr Tyr Val Thr Asn Leu Asn Ala Ala Leu Glu Gly His Pro Asp 35 40 45

Leu Gln Asn Lys Ser Leu Glu Glu Leu Leu Ser Asn Leu Glu Ala Leu
50 55 60

Pro Glu Ser Ile Arg Thr Ala Val Arg Asn Asn Gly Gly His Ala 65 70 75 80

Asn His Ser Leu Phe Trp Thr Ile Leu Ser Pro Asn Gly Gly Glu 85 90 95

Pro Thr Gly Glu Leu Ala Asp Ala Ile Asn Lys Lys Phe Gly Ser Phe 100 105 110

Thr Ala Phe Lys Asp Glu Phe Ser Lys Ala Ala Ala Gly Arg Phe Gly
115 120 125

Ser Gly Trp Ala Trp Leu Val Val Asn Asn Gly Glu Leu Glu Ile Thr 130 135 140

Ser Thr Pro Asn Gln Asp Ser Pro Ile Met Glu Gly Lys Thr Pro Ile 145 150 155 160

Leu Gly Leu Asp Val Trp Glu His Ala Tyr Tyr Leu Lys Tyr Gln Asn 165 170 175

Arg Arg Pro Glu Tyr Ile Ala Ala Phe Trp Asn Val Val Asn Trp Asp 180 185 190

Glu Val Ala Lys Arg Tyr Ser Glu Ala Lys Ala Lys Gln Arg Ser Cys 195 200 205

Gly Leu Val Pro Arg Gly Ser Gly Pro Gly Ser Lys Ala Pro Pro Arg 210 215 220

Leu Cys Ile Arg Val Asn Asn Arg Glu Leu Phe Phe Val Ala Ser Glu 225 230 235 240

Ser Ser Tyr Asn Glu Asn Asp Ile Asn Thr Pro Lys Glu Ile Asp Asp 245 250 255

Thr Thr Asn Leu Asn Asn Asn Tyr Arg Asn Asn Leu Asp Glu Val Ile

260 265 270 Leu Asp Tyr Asn Ser Glu Thr Ile Pro Gln Ile Ser Asn Gln Thr Leu 275 280 Asn Thr Leu Val Gln Asp Asp Ser Tyr Val Pro Arg Tyr Asp Ser Asn Gly Thr Ser Glu Ile Glu Glu His Asn Val Val Asp Leu Asn Val Phe 315 Phe Tyr Leu His Ala Gln Lys Val Pro Glu Gly Glu Thr Asn Ile Ser 330 Leu Thr Ser Ser Ile Asp Thr Ala Leu Ser Glu Glu Ser Gln Val Tyr 340 345 Thr Phe Phe Ser Ser Glu Phe Ile Asn Thr Ile Asn Lys Pro Val His Ala Ala Leu Phe Ile Ser Trp Ile Asn Gln Val Ile Arg Asp Phe Thr 375 Thr Glu Ala Thr Gln Lys Ser Thr Phe Asp Lys Ile Ala Asp Ile Ser 385 390 395 Leu Val Val Pro Tyr Val Gly Leu Ala Leu Asn Ile Gly Asn Glu Val 410 Gln Lys Glu Asn Phe Lys Glu Ala Phe Glu Leu Leu Gly Ala Gly Ile 425 Leu Leu Glu Phe Val Pro Glu Leu Leu Ile Pro Thr Ile Leu Val Phe Thr Ile Lys Ser Phe Ile Gly Ser Ser Glu Asn Lys Asn Lys Ile Ile 455 Lys Ala Ile Asn Asn Ser Leu Met Glu Arg Glu Thr Lys Trp Lys Glu 475 Ile Tyr Ser Trp Ile Val Ser Asn Trp Leu Thr Arg Ile Asn Thr Gln Phe Asn Lys Arg Lys Glu Gln Met Tyr Gln Ala Leu Gln Asn Gln Val 500 505 Asp Ala Ile Lys Thr Val Ile Glu Tyr Lys Tyr Asn Asn Tyr Thr Ser Asp Glu Arg Asn Arg Leu Glu Ser Glu Tyr Asn Ile Asn Asn Ile Arg Glu Glu Leu Asn Lys Lys Val Ser Leu Ala Met Glu Asn Ile Glu Arq 550 Phe Ile Thr Glu Ser Ser Ile Phe Tyr Leu Met Lys Leu Ile Asn Glu

Leu Leu Asp Tyr Ile Ser Glu His Arg Ser Ile Leu Gly Asn Ser Val
595
600
605
Gln Glu Leu Asn Asp Leu Val Thr Ser Thr Leu Asn Asn Ser Ile Pro

Ala Lys Val Ser Lys Leu Arg Glu Tyr Asp Glu Gly Val Lys Glu Tyr

610 615 620

Phe Glu Leu Ser Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe 630 635 Asn Lys Leu Tyr Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg 650 Tyr Glu Asn Asn Lys Phe Ile Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn Gly Asp Val Tyr Ile Tyr Ser Thr Asn Arg Asn Gln Phe Gly Ile Tyr Ser Ser Lys Pro Ser Glu Val Asn Ile Ala Gln Asn Asn 695 Asp Ile Ile Tyr Asn Gly Arg Tyr Gln Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro Lys Tyr Phe Asn Lys Val Asn Leu Asn Asn Glu Tyr Thr Ile Ile Asp Cys Ile Arg Asn Asn Asn Ser Gly Trp Lys Ile Ser 745 Leu Asn Tyr Asn Lys Ile Ile Trp Thr Leu Gln Asp Thr Ala Gly Asn Asn Gln Lys Leu Val Phe Asn Tyr Thr Gln Met Ile Ser Ile Ser Asp 775 Tyr Ile Asn Lys Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Gly 795 Asn Ser Arg Ile Tyr Ile Asn Gly Asn Leu Ile Asp Glu Lys Ser Ile 810 Ser Asn Leu Gly Asp Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile 825 Val Gly Cys Asn Asp Thr Arg Tyr Val Gly Ile Arg Tyr Phe Lys Val Phe Asp Thr Glu Leu Gly Lys Thr Glu Ile Glu Thr Leu Tyr Ser Asp 855 Glu Pro Asp Pro Ser Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu 875 Tyr Asn Lys Arg Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln Asn Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val 905 Tyr Gln Lys Pro Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile Ile Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val Arg Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg 950 955 Asp Val Glu Tyr Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu 965 970 975

Lys Ile Ile Lys Leu Ile Arg Thr Ser Asn Ser Asn Ser Leu Gly 980 985 990

Gln Ile Ile Val Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe 995 1000 1005

Gln Asn Asn Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn 1010 1015 1020

Asn Leu Val Ala Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr 1025 1030 1035 1040

Ser Ser Asn Gly Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp 1045 1050 1055

Gln Glu Asn

<210> 6

<211> 1092

<212> PRT

<213> Artificial Sequence

<220h

<223> Description of Artificial Sequence:construct

<400> 6

Met Leu Ser Arg Ala Val Cys Gly Thr Ser Arg Gln Leu Ala Pro Ala 1 5 10 15

Leu Gly Tyr Leu Gly Ser Arg Gln Lys His Ser Arg Gly Ser Pro Ala
20 25 30

Leu Pro Tyr Pro Tyr Asp Ala Leu Glu Pro His Ile Asp Lys Glu Thr 35 40 45

Met Asn Ile His His Thr Lys His His Asn Thr Tyr Val Thr Asn Leu 50 60

Asn Ala Ala Leu Glu Gly His Pro Asp Leu Gln Asn Lys Ser Leu Glu 65 70 75 80

Glu Leu Leu Ser Asn Leu Glu Ala Leu Pro Glu Ser Ile Arg Thr Ala 85 90 95

Val Arg Asn Asn Gly Gly His Ala Asn His Ser Leu Phe Trp Thr

Ile Leu Ser Pro Asn Gly Gly Gly Glu Pro Thr Gly Glu Leu Ala Asp 115 120 125

Ala Ile Asn Lys Lys Phe Gly Ser Phe Thr Ala Phe Lys Asp Glu Phe 130 135 140

Ser Lys Ala Ala Ala Gly Arg Phe Gly Ser Gly Trp Ala Trp Leu Val 145 150 155 160

Val Asn Asn Gly Glu Leu Glu Ile Thr Ser Thr Pro Asn Gln Asp Ser 165 170 175

Pro Ile Met Glu Gly Lys Thr Pro Ile Leu Gly Leu Asp Val Trp Glu 180 185 190 His Ala Tyr Tyr Leu Lys Tyr Gln Asn Arg Arg Pro Glu Tyr Ile Ala Ala Phe Trp Asn Val Val Asn Trp Asp Glu Val Ala Lys Arg Tyr Ser 215 Glu Ala Lys Ala Lys Gln Arg Ser Cys Gly Leu Val Pro Arg Gly Ser Gly Pro Gly Ser Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu 280 Asn Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile 315 Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly 325 330 Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu 395 Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr 420 425 Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe 440 Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr 475 Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser 485 490 Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn

535

Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala 565 570 Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp 600 Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr 630 635 Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Asn Ile Ile Asn Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp Leu Ser 680 Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys Ile 710 715 Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu Asn 725 Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser Ile 745 Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu Gln 770 Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln Met 795 Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu Ile 825 Asp Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn Asn 840 Ile Met Phe Lys Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp Phe 885 890 895

Trp Gly Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr Met Leu Asn Leu 900 905 910

Tyr Asp Pro Asn Lys Tyr Val Asp Val Asn Asn Val Gly Ile Arg Gly 915 920 925

Tyr Met Tyr Leu Lys Gly Pro Arg Gly Ser Val Met Thr Thr Asn Ile 930 935 940

Tyr Leu Asn Ser Ser Leu Tyr Arg Gly Thr Lys Phe Ile Ile Lys Lys 945 950 955 960

Tyr Ala Ser Gly Asn Lys Asp Asn Ile Val Arg Asn Asp Arg Val 965 970 975

Tyr Ile Asn Val Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr Asn 980 985 990

Ala Ser Gln Ala Gly Val Glu Lys Ile Leu Ser Ala Leu Glu Ile Pro 995 1000 1005

Asp Val Gly Asn Leu Ser Gln Val Val Met Lys Ser Lys Asn Asp 1010 1015 1020

Gln Gly Ile Thr Asn Lys Cys Lys Met Asn Leu Gln Asp Asn Asn Gly 1025 1030 1035 1040

Asn Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn Asn Ile Ala Lys
1045 1050 1055

Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser Arg
1060 1065 1070

Thr Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp Asp Gly Trp Gly 1075 1080 1085

Glu Arg Pro Leu 1090

<210> 7

<211> 1095

<212> PRT

<213> Artificial Sequence

<220×

<223> Description of Artificial Sequence:construct

<400> 7

Met Leu Ser Arg Ala Val Cys Gly Thr Ser Arg Gln Leu Ala Pro Ala 1 5 10 15

Leu Gly Tyr Leu Gly Ser Arg Gln Lys His Ser Arg Gly Ser Pro Ala 20 25 30

Leu Pro Tyr Pro Tyr Asp Ala Leu Glu Pro His Ile Asp Lys Glu Thr 35 40

Met Asn Ile His His Thr Lys His His Asn Thr Tyr Val Thr Asn Leu 50 55 60

Asn Ala Ala Leu Glu Gly His Pro Asp Leu Gln Asn Lys Ser Leu Glu 65 70 75 80

Glu Leu Leu Ser Asn Leu Glu Ala Leu Pro Glu Ser Ile Arg Thr Ala

85 90 95

Val Arg Asn Asn Gly Gly His Ala Asn His Ser Leu Phe Trp Thr Ile Leu Ser Pro Asn Gly Gly Glu Pro Thr Gly Glu Leu Ala Asp Ala Ile Asn Lys Lys Phe Gly Ser Phe Thr Ala Phe Lys Asp Glu Phe Ser Lys Ala Ala Ala Gly Arg Phe Gly Ser Gly Trp Ala Trp Leu Val 155 Val Asn Asn Gly Glu Leu Glu Ile Thr Ser Thr Pro Asn Gln Asp Ser 165 170 Pro Ile Met Glu Gly Lys Thr Pro Ile Leu Gly Leu Asp Val Trp Glu 185 His Ala Tyr Tyr Leu Lys Tyr Gln Asn Arg Arg Pro Glu Tyr Ile Ala Ala Phe Trp Asn Val Val Asn Trp Asp Glu Val Ala Lys Arg Tyr Ser Glu Ala Lys Ala Lys Gln Arg Ser Cys Gly Leu Val Pro Arg Gly Ser 235 Gly Pro Gly Ser Lys Ala Pro Gly Ile Cys Ile Asp Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu Ser 265 Lys Asn Glu Arg Ile Glu Tyr Asn Thr Gln Ser Asn Tyr Ile Glu Asn 280 Asp Phe Pro Ile Asn Glu Leu Ile Leu Asp Thr Asp Leu Ile Ser Lys Ile Glu Leu Pro Ser Glu Asn Thr Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val Tyr Glu Lys Gln Pro Ala Ile Lys Lys Ile Phe Thr 325 330 Asp Glu Asn Thr Ile Phe Gln Tyr Leu Tyr Ser Gln Thr Phe Pro Leu 345 Asp Ile Arg Asp Ile Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn Lys Val Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys Gln 390 395 Ile Val Asn Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met Asp 410 Lys Ile Ala Asp Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala Leu 425 Asn Val Gly Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe Glu

435 440 445

Ile Ala Gly Ala Ser Ile Leu Leu Glu Phe Ile Pro Glu Leu Leu Ile 455 Pro Val Val Gly Ala Phe Leu Leu Glu Ser Tyr Ile Asp Asn Lys Asn 470 Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser Thr Val 505 Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile Asn 565 Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile 585 Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys 595 Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser 615 Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr Ile Met 630 635 Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile Leu Ile Glu Met Phe Asn Lys Tyr Asn Ser Glu Ile Leu Asn Asn Ile Ile Leu Asn Leu 665 Arg Tyr Lys Asp Asn Asn Leu Ile Asp Leu Ser Gly Tyr Gly Ala Lys 675 680 685 Val Glu Val Tyr Asp Gly Val Glu Leu Asn Asp Lys Asn Gln Phe Lys Leu Thr Ser Ser Ala Asn Ser Lys Ile Arg Val Thr Gln Asn Gln Asn 705 Ile Ile Phe Asn Ser Val Phe Leu Asp Phe Ser Val Ser Phe Trp Ile Arg Ile Pro Lys Tyr Lys Asn Asp Gly Ile Gln Asn Tyr Ile His Asn 745 Glu Tyr Thr Ile Ile Asn Cys Met Lys Asn Asn Ser Gly Trp Lys Ile Ser Ile Arg Gly Asn Arg Ile Ile Trp Thr Leu Ile Asp Ile Asn Gly 775 Lys Thr Lys Ser Val Phe Phe Glu Tyr Asn Ile Arg Glu Asp Ile Ser

790 795 800 Glu Tyr Ile Asn Arg Trp Phe Phe Val Thr Ile Thr Asn Asn Leu Asn Asn Ala Lys Ile Tyr Ile Asn Gly Lys Leu Glu Ser Asn Thr Asp Ile 825 Lys Asp Ile Arg Glu Val Ile Ala Asn Gly Glu Ile Ile Phe Lys Leu Asp Gly Asp Ile Asp Arg Thr Gln Phe Ile Trp Met Lys Tyr Phe Ser 855 Ile Phe Asn Thr Glu Leu Ser Gln Ser Asn Ile Glu Glu Arg Tyr Lys 875 870 Ile Gln Ser Tyr Ser Glu Tyr Leu Lys Asp Phe Trp Gly Asn Pro Leu Met Tyr Asn Lys Glu Tyr Tyr Met Phe Asn Ala Gly Asn Lys Asn Ser Tyr Ile Lys Leu Lys Lys Asp Ser Pro Val Gly Glu Ile Leu Thr Arg 920 Ser Lys Tyr Asn Gln Asn Ser Lys Tyr Ile Asn Tyr Arg Asp Leu Tyr 935 Ile Gly Glu Lys Phe Ile Ile Arg Arg Lys Ser Asn Ser Gln Ser Ile Asn Asp Asp Ile Val Arg Lys Glu Asp Tyr Ile Tyr Leu Asp Phe Phe Asn Leu Asn Gln Glu Trp Arg Val Tyr Thr Tyr Lys Tyr Phe Lys Lys Glu Glu Glu Lys Leu Phe Leu Ala Pro Ile Ser Asp Ser Asp Glu Phe 1000 1005 Tyr Asn Thr Ile Gln Ile Lys Glu Tyr Asp Glu Gln Pro Thr Tyr Ser 1015 Cys Gln Leu Leu Phe Lys Lys Asp Glu Glu Ser Thr Asp Glu Ile Gly 1035 1030 Leu Ile Gly Ile His Arg Phe Tyr Glu Ser Gly Ile Val Phe Glu Glu 1050 Tyr Lys Asp Tyr Phe Cys Ile Ser Lys Trp Tyr Leu Lys Glu Val Lys 1065 Arg Lys Pro Tyr Asn Leu Lys Leu Gly Cys Asn Trp Gln Phe Ile Pro 1080

<210> 8

1090

Lys Asp Glu Gly Trp Thr Glu

<sup>&</sup>lt;211> 1084

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:construct

<400> 8

Met Leu Ser Arg Ala Val Cys Gly Thr Ser Arg Gln Leu Ala Pro Ala 1 5 10 15

Leu Gly Tyr Leu Gly Ser Arg Gln Lys His Ser Arg Gly Ser Pro Ala 20 25 30

Leu Pro Tyr Pro Tyr Asp Ala Leu Glu Pro His Ile Asp Lys Glu Thr
35 40 45

Met Asn Ile His His Thr Lys His His Asn Thr Tyr Val Thr Asn Leu 50 55 60

Asn Ala Ala Leu Glu Gly His Pro Asp Leu Gln Asn Lys Ser Leu Glu 65 70 75 80

Glu Leu Leu Ser Asn Leu Glu Ala Leu Pro Glu Ser Ile Arg Thr Ala 85 90 95

Val Arg Asn Asn Gly Gly Gly His Ala Asn His Ser Leu Phe Trp Thr
100 105 110

Ile Leu Ser Pro Asn Gly Gly Glu Pro Thr Gly Glu Leu Ala Asp 115 120 125

Ala Ile Asn Lys Lys Phe Gly Ser Phe Thr Ala Phe Lys Asp Glu Phe 130 135 140

Ser Lys Ala Ala Ala Gly Arg Phe Gly Ser Gly Trp Ala Trp Leu Val 145 150 155 160

Val Asn Asn Gly Glu Leu Glu Ile Thr Ser Thr Pro Asn Gln Asp Ser 165 170 175

Pro Ile Met Glu Gly Lys Thr Pro Ile Leu Gly Leu Asp Val Trp Glu 180 185 190

His Ala Tyr Tyr Leu Lys Tyr Gln Asn Arg Arg Pro Glu Tyr Ile Ala 195 200 205

Ala Phe Trp Asn Val Val Asn Trp Asp Glu Val Ala Lys Arg Tyr Ser 210 215 220

Glu Ala Lys Ala Lys Gln Arg Ser Cys Gly Leu Val Pro Arg Gly Ser 225 230 235 240

Gly Pro Gly Ser Lys Ala Pro Pro Arg Leu Cys Ile Arg Val Asn Asn 245 250 255

Ile Asn Thr Pro Lys Glu Ile Asp Asp Thr Thr Asn Leu Asn Asn Asn 275 280 285

Tyr Arg Asn Asn Leu Asp Glu Val Ile Leu Asp Tyr Asn Ser Glu Thr 290 295 300

Ile Pro Gln Ile Ser Asn Gln Thr Leu Asn Thr Leu Val Gln Asp Asp 305 310 315 320

Ser Tyr Val Pro Arg Tyr Asp Ser Asn Gly Thr Ser Glu Ile Glu Glu 325 330 335

His Asn Val Val Asp Leu Asn Val Phe Phe Tyr Leu His Ala Gln Lys Val Pro Glu Gly Glu Thr Asn Ile Ser Leu Thr Ser Ser Ile Asp Thr 360 Ala Leu Ser Glu Glu Ser Gln Val Tyr Thr Phe Phe Ser Ser Glu Phe Ile Asn Thr Ile Asn Lys Pro Val His Ala Ala Leu Phe Ile Ser Trp 390 395 Ile Asn Gln Val Ile Arg Asp Phe Thr Thr Glu Ala Thr Gln Lys Ser 405 410 Thr Phe Asp Lys Ile Ala Asp Ile Ser Leu Val Val Pro Tyr Val Gly 425 Leu Ala Leu Asn Ile Gly Asn Glu Val Gln Lys Glu Asn Phe Lys Glu Ala Phe Glu Leu Gly Ala Gly Ile Leu Leu Glu Phe Val Pro Glu 455 Leu Leu Ile Pro Thr Ile Leu Val Phe Thr Ile Lys Ser Phe Ile Gly 470 475 Ser Ser Glu Asn Lys Asn Lys Ile Ile Lys Ala Ile Asn Asn Ser Leu 485 Met Glu Arg Glu Thr Lys Trp Lys Glu Ile Tyr Ser Trp Ile Val Ser 505 Asn Trp Leu Thr Arg Ile Asn Thr Gln Phe Asn Lys Arg Lys Glu Gln 520 Met Tyr Gln Ala Leu Gln Asn Gln Val Asp Ala Ile Lys Thr Val Ile 535 Glu Tyr Lys Tyr Asn Asn Tyr Thr Ser Asp Glu Arg Asn Arg Leu Glu Ser Glu Tyr Asn Ile Asn Asn Ile Arg Glu Glu Leu Asn Lys Lys Val 565 Ser Leu Ala Met Glu Asn Ile Glu Arg Phe Ile Thr Glu Ser Ser Ile Phe Tyr Leu Met Lys Leu Ile Asn Glu Ala Lys Val Ser Lys Leu Arg Glu Tyr Asp Glu Gly Val Lys Glu Tyr Leu Leu Asp Tyr Ile Ser Glu His Arg Ser Ile Leu Gly Asn Ser Val Gln Glu Leu Asn Asp Leu Val 630 635 Thr Ser Thr Leu Asn Asn Ser Ile Pro Phe Glu Leu Ser Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn Lys Leu Tyr Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg Tyr Glu Asn Asn Lys Phe Ile 680

Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn Gly Asp Val Tyr Ile Tyr Ser Thr Asn Arg Asn Gln Phe Gly Ile Tyr Ser Ser Lys Pro 715 Ser Glu Val Asn Ile Ala Gln Asn Asn Asp Ile Ile Tyr Asn Gly Arg Tyr Gln Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro Lys Tyr Phe 745 Asn Lys Val Asn Leu Asn Asn Glu Tyr Thr Ile Ile Asp Cys Ile Arg 760 Asn Asn Asn Ser Gly Trp Lys Ile Ser Leu Asn Tyr Asn Lys Ile Ile Trp Thr Leu Gln Asp Thr Ala Gly Asn Asn Gln Lys Leu Val Phe Asn 795 Tyr Thr Gln Met Ile Ser Ile Ser Asp Tyr Ile Asn Lys Trp Ile Phe 805 Val Thr Ile Thr Asn Asn Arg Leu Gly Asn Ser Arg Ile Tyr Ile Asn 825 Gly Asn Leu Ile Asp Glu Lys Ser Ile Ser Asn Leu Gly Asp Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val Gly Cys Asn Asp Thr Arg 855 Tyr Val Gly Ile Arg Tyr Phe Lys Val Phe Asp Thr Glu Leu Gly Lys 870 875 Thr Glu Ile Glu Thr Leu Tyr Ser Asp Glu Pro Asp Pro Ser Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asn Lys Arg Tyr Tyr Leu 905 Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln Asn Ser Asn Phe 915 925 Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys Pro Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile Ile Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val Arg Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu Tyr Arg Leu Tyr 985 Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile Lys Leu Ile Arg 1000 Thr Ser Asn Ser Asn Ser Leu Gly Gln Ile Ile Val Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn Asn Gly Gly Asn

1030

Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val Ala Ser Ser Trp 1045 1050 1055

Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn Gly Cys Phe Trp
1060 1065 1070

Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn 1075 1080

<210> 9

<211> 229

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: polypeptide comprising a mitochondrial leader from human MnSOD and B. Stearothermophilus SOS

<400> 9

Met Leu Ser Arg Ala Val Cys Gly Thr Ser Arg Gln Leu Ala Pro Ala 1 5 10 15

Leu Gly Tyr Leu Gly Ser Arg Gln Lys His Ser Arg Gly Ser Pro Ala 20 25 30

Leu Pro Tyr Pro Tyr Asp Ala Leu Glu Pro His Ile Asp Lys Glu Thr 35 40 45

Met Asn Ile His His Thr Lys His His Asn Thr Tyr Val Thr Asn Leu
50 60

Asn Ala Ala Leu Glu Gly His Pro Asp Leu Gln Asn Lys Ser Leu Glu 65 70 75 80

Glu Leu Leu Ser Asn Leu Glu Ala Leu Pro Glu Ser Ile Arg Thr Ala 85 90 95

Val Arg Asn Asn Gly Gly His Ala Asn His Ser Leu Phe Trp Thr 100 105 110

Ile Leu Ser Pro Asn Gly Gly Glu Pro Thr Gly Glu Leu Ala Asp 115 120 125

Ala Ile Asn Lys Lys Phe Gly Ser Phe Thr Ala Phe Lys Asp Glu Phe 130 140

Ser Lys Ala Ala Gly Arg Phe Gly Ser Gly Trp Ala Trp Leu Val 145 150 155 160

Val Asn Asn Gly Glu Leu Glu Ile Thr Ser Thr Pro Asn Gln Asp Ser 165 170 175

Pro Ile Met Glu Gly Lys Thr Pro Ile Leu Gly Leu Asp Val Trp Glu
180 185 190

His Ala Tyr Tyr Leu Lys Tyr Gln Asn Arg Arg Pro Glu Tyr Ile Ala 195 200 205

Ala Phe Trp Asn Val Val Asn Trp Asp Glu Val Ala Lys Arg Tyr Ser 210 215 220

Glu Ala Lys Ala Lys

```
<210> 10
<211> 24
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: modified human
      mitocondrial leader sequence
<400> 10
Met Leu Ser Arg Ala Val Ser Gly Thr Ser Arg Gln Leu Ala Pro Ala
Leu Gly Tyr Leu Gly Ser Arg Gln
             20
<210> 11
<211> 24
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: modified human
      mitochondrial leader sequence
<400> 11
Met Leu Ser Arg Ala Val Cys Gly Thr Ser Arg Gln Leu Ala Pro Ala
                                      10
Leu Gly Tyr Leu Gly Ser Arg Gln
             20
<210> 12
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: linker peptide
<400> 12
Cys Gly Leu Val Pro Ala Gly Ser Gly Pro
<210> 13
<211> 27
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: modified human
      mitocondrial leader sequence
<400> 13
Met Leu Ser Arg Ala Val Cys Gly Thr Ser Arg Gln Leu Ala Pro Ala
Leu Gly Tyr Leu Gly Ser Arg Gln Lys His Ser
```

<210> 14

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: modified human mitochondrial leader sequence

<400> 14

Met Leu Ser Arg Ala Val Ser Gly Thr Ser Arg Gln Leu Ala Pro Ala 1 5 10 15

Leu Gly Tyr Leu Gly Ser Arg Gln Lys His Ser 20 25